Amendments to the Claims

The following listing of claims will replace all prior versions, and listings, of claims in this application.

Listing of claims:

1. - 36. (cancelled)

37. (currently amended) A method for identifying a compound capable of binding to the CD4 binding site of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 comprising:

a. determining the CD4 binding site on [[the]] gp120 based on the atomic coordinates computed from X-ray diffraction data of a crystal ~~comprising a polypeptide having amino acid sequence of a portion of gp120 capable of binding to CD4~~ suitable for X-ray diffraction, which crystal comprises a complex of:

(i) a deglycosylated polypeptide having an amino acid sequence of a variant of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 which sequence comprises, in the following order:

a) amino acid residues 83-127 of mature gp120;

b) amino acids GAG;

c) amino acid residues 195-302 of mature gp120;

d) amino acids GAG; and

e) amino acid residues 330-492; and

(ii) a polypeptide having an amino acid sequence of the N-terminal D1D2 domains of CD4 comprising amino acid residues 1-182, and

(iii) an antigen-binding fragment (Fab) of a monoclonal antibody designated 17b to a discontinuous epitope of gp120,

wherein the crystal effectively diffracts X-rays for determination of the atomic coordinates of the gp120 polypeptide to a resolution of 2.5 angstroms or better than 2.5 angstroms; [[and]]

b. comparing the structure of the CD4 binding site determined from step (a) with the structure of a compound; and

[[b.]] c. determining whether the compound would fit into the binding site, a positive fitting indicating that the compound is capable of binding to the CD4 binding site of gp120.

38. (currently amended) A method for designing a compound capable of binding to the CD4 binding site of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 comprising:

a. determining the CD4 binding site on [[the]] gp120 based on the atomic coordinates computed from X-ray diffraction data of a crystal ~~comprising a polypeptide having amino acid sequence of a portion of gp120 capable of binding to CD4~~ suitable for X-ray diffraction, which crystal comprises a complex of:

(i) a deglycosylated polypeptide having an amino acid sequence of a variant of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 which sequence comprises, in the following order:

a) amino acid residues 83-127 of mature gp120;

b) amino acids GAG;

c) amino acid residues 195-302 of mature gp120;

d) amino acids GAG; and

e) amino acid residues 330-492; and

(ii) a polypeptide having an amino acid sequence of the N-terminal D1D2 domains of CD4 comprising amino acid residues 1-182, and

(iii) an antigen-binding fragment (Fab) of a monoclonal antibody designated 17b to a discontinuous epitope of gp120,

wherein the crystal effectively diffracts X-rays for determination of the atomic coordinates of the gp120 polypeptide to a resolution of 2.5 angstroms or better than 2.5 angstroms; and

b. designing a compound to fit the CD4 binding site determined from step (a).

39. - 96. (cancelled)

97. (new) A method for identifying a compound capable of binding to the CD4 binding site of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 comprising:

a. determining the CD4 binding site on gp120 based on the atomic coordinates computed from X-ray

diffraction data of a crystal suitable for X-ray diffraction, which crystal comprises a complex of:

(i) a deglycosylated polypeptide having an amino acid sequence of a variant of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 which sequence comprises amino acid residues 90-396 and 410-492 except loop substitutions of mature gp120; and

(ii) a polypeptide having an amino acid sequence of the N-terminal D1D2 domains of CD4 comprising amino acid residues 1-181, and

(iii) a polypeptide having an amino acid sequence of an antigen-binding fragment (Fab) of a monoclonal antibody designated 17b comprising amino acid residues 1-213 of the light chain and amino acid residues 1-229 of the heavy chain,

wherein the crystal effectively diffracts X-rays for determination of the atomic coordinates of the gp120 polypeptide to a resolution of 2.5 angstroms or better than 2.5 angstroms;

b. comparing the structure of the CD4 binding site determined from step (a) with the structure of a compound; and

c. determining whether the compound would fit into the binding site, a positive fitting indicating that the compound is capable of binding to the CD4 binding site of gp120.

98. (new) A method for designing a compound capable of binding to the CD4 binding site of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 comprising:

a. determining the CD4 binding site on gp120 based on the atomic coordinates computed from X-ray diffraction data of a crystal suitable for X-ray diffraction, which crystal comprises a complex of:

(i) a deglycosylated polypeptide having an amino acid sequence of a variant of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 which sequence comprises amino acid residues 90-396 and 410-492 except loop substitutions of mature gp120; and

(ii) a polypeptide having an amino acid sequence of the N-terminal D1D2 domains of CD4 comprising amino acid residues 1-181, and

(iii) a polypeptide having an amino acid sequence of an antigen-binding fragment (Fab) of a monoclonal antibody designated 17b comprising amino acid residues 1-213 of the light chain and amino acid residues 1-229 of the heavy chain,

wherein the crystal effectively diffracts X-rays for determination of the atomic coordinates of the gp120 polypeptide to a resolution of 2.5 angstroms or better than 2.5 angstroms; and

b. designing a compound to fit the CD4 binding site determined from step (a).

99. (new) A method for identifying a compound capable of binding to the CD4 binding site of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 comprising:

a. determining the CD4 binding site on gp120 based on the atomic coordinates computed from X-ray diffraction data of a crystal suitable for X-ray diffraction, which crystal comprises a complex of:

(i) a deglycosylated polypeptide having an amino acid sequence of a Human Immunodeficiency Virus Type I envelope glycoprotein gp120 construct Δ82ΔV1/2*ΔV3ΔC5; and

(ii) a polypeptide having an amino acid sequence of the N-terminal D1D2 domains of CD4; and

(iii) a polypeptide having an amino acid sequence of an antigen-binding fragment (Fab) of a monoclonal antibody designated 17b,

wherein the crystal effectively diffracts X-rays for determination of the atomic coordinates of the gp120 polypeptide to a resolution of 2.5 angstroms or better than 2.5 angstroms;

b. comparing the structure of the CD4 binding site determined from step (a) with the structure of a compound; and

c. determining whether the compound would fit into the binding site, a positive fitting indicating that the compound is capable of binding to the CD4 binding site of gp120.

100. (new) A method for designing a compound capable of binding to the CD4 binding site of Human Immunodeficiency Virus Type I envelope glycoprotein gp120 comprising:

a. determining the CD4 binding site on gp120 based on the atomic coordinates computed from X-ray diffraction data of a crystal suitable for X-ray diffraction, which crystal comprises a complex of:

(i) a deglycosylated polypeptide having an amino acid sequence of a Human Immunodeficiency Virus Type I envelope glycoprotein gp120 construct Δ82ΔV1/2*ΔV3ΔC5; and

(ii) a polypeptide having an amino acid sequence of the N-terminal D1D2 domains of CD4; and

(iii) a polypeptide having an amino acid sequence of an antigen-binding fragment (Fab) of a monoclonal antibody designated 17b,

wherein the crystal effectively diffracts X-rays for determination of the atomic coordinates of the gp120 polypeptide to a resolution of 2.5 angstroms or better than 2.5 angstroms; and

b. designing a compound to fit the CD4 binding site determined from step (a).

101. (new) The method of claim 37, wherein the fitting is determined by shape complementarity or by estimated interaction energy.

102. (new) The method of claim 38, wherein the fitting is determined by shape complementarity or by estimated interaction energy.

103. (new) The method of claim 97, wherein the fitting is determined by shape complementarity or by estimated interaction energy.

104. (new) The method of claim 98, wherein the fitting is determined by shape complementarity or by estimated interaction energy.

105. (new) The method of claim 99, wherein the fitting is determined by shape complementarity or by estimated interaction energy.

106. (new) The method of claim 100, wherein the fitting is determined by shape complementarity or by estimated interaction energy.